Attorney Docket No.: MEDIV2010-2

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In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:

Please amend claims 1, 7-8, 31, 87, 90, 95 and 103as follows:

1. (Currently Amended) A method of enhancing collateral blood vessel formation in a

subject comprising

directly administering to sites in heart or limb tissue a composition comprising an effective

amount of autologous bone marrow aspirate to induce collateral blood vessel formation in the

tissue.

2. (Previously Presented) The method of claim 1, wherein the autologous bone marrow

aspirate is injected.

3. (Previously Presented) The method of claim 1, wherein the autologous bone marrow

aspirate is injected intramyocardially.

4. (Previously Presented) The method of claim [[3]] 2 wherein the wherein the autologous

bone marrow aspirate is injected trans-epicardially or trans-endocardially.

5. (Previously Presented) The method of claim 4, wherein the trans-endocardial approach is

via a catheter.

6. (Cancelled)

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- 7. (Currently Amended) The method of claim 1, wherein the autologous bone marrow aspirate has been stimulated while growing in conditioned medium ex vivo, the conditioned medium comprising [[of]] at least one agent selected from granulocyte-monocyte colony stimulating factor (GM-CSF), endothelial PAS domain 1 (EPAS1) and hypoxia inducible factor 1 (HIF-1).
- 8. (Currently Amended) The method of claim 7, wherein the autologous bone marrow aspirate has been stimulated by contact with one or more angiogenesis stimulating cytokines secreted therefrom while growing in conditioned medium ex vivo, the conditioned medium comprising [[of]] at least one agent selected from granulocyte-monocyte colony stimulating factor (GM-CSF), endothelial PAS domain 1 (EPAS1) and hypoxia inducible factor 1 (HIF-1).
- 9. (Previously Presented) The method of claim 1, wherein the composition further comprises Monocyte Chemoattractant Protein 1 (MCP-1) or Vascular Endothelial Growth Factor (VEGF).

Claims 10-11 (Cancelled)

- 12. (Previously Presented) The method of claim 7, wherein the autologous bone marrow aspirate has been stimulated ex vivo in culture by transient exposure to hypoxia.
- 13. (Cancelled)
- 14. (Currently Amended) The method of claim 1, wherein the autologous bone marrow aspirate is administered in combination with one or more agent selected from a pharmacological drug, or protein, or gene that enhances bone marrow production of angiogenic growth factors selected to promote endothelial cell proliferation, migration, or blood vessel formation.

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- 15. (Previously Presented) The method of claim 14, wherein the autologous bone marrow aspirate and the agent or agents are administered together.
- 16. (Previously Presented) The method of claim 14, wherein the autologous bone marrow aspirate and the agent or agents are combined ex vivo prior to administration.
- 17. (Currently Amended) The method of claim 16, wherein the autologous bone marrow aspirate has been stimulated ex vivo in conditioned medium, the conditioned medium comprising [[of]] at least one agent selected from granulocyte-monocyte colony stimulating factor (GM-CSF), endothelial PAS domain 1 (EPAS1) and hypoxia inducible factor 1 (HIF-1).
- 18. (Currently Amended) The method of claim 1, wherein the composition is administered to ischemic tissue is treated.

Claims 19-30 (Cancelled)

31. (Currently Amended) The method of claim [17] 16, further comprising culturing the autologous bone marrow aspirate prior to (b) to form conditioned medium containing bone marrow cells and endogenously secreted angiogenic cytokines and injecting the composition into ischemic heart tissue.

Claims 32-86 (Cancelled)

87. (Currently Amended) A composition <u>for enhancing collateral blood vessel development</u> comprising cultured autologous bone marrow aspirate that has been stimulated ex vivo by

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exposure to hypoxia or an <u>effective amount of at least one</u> angiogenesis stimulating cytokine selected from <u>GM-CSF</u>, <u>MCP-1</u>, <u>EPAS1</u> and <u>HIF-1</u>.

Claims 88-89 (Cancelled)

90. (Currently Amended) The composition of claim 87, wherein the cytokine is MCP-1.

Claims 91-93 (Cancelled)

- 94. (Previously Presented) The composition of claim 87, further comprising conditioned medium in which the autologous bone marrow aspirate has been grown.
- 95. (Currently Amended) The composition of claim <u>87</u>, further comprising a pharmacological drug or protein that enhances bone marrow production of angiogenic growth factors and/or promotes endothelial cell proliferation, migration, or blood vessel formation.
- 96. (Previously Presented) The composition of claim 87, which further comprises heparin or another anticoagulant.

Claims 97-102 (Cancelled)

103. (Currently Amended) A method of enhancing collateral blood vessel formation in a subject in need thereof comprising directly administering to <u>ischemic</u> sites in heart or limb tissue of the subject an effective amount of conditioned medium in which <u>autologous</u> bone marrow aspirate has been grown <u>in cell growth medium under hypoxia or wherein the growth medium</u> comprises an effective amount of at least one angiogenesis stimulating cytokine selected from

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<u>GM-CSF, MCP-1, EPAS1 and HIF-1</u> to induce collateral blood vessel formation in the heart or limb tissue.

Please add the following new claims:

- 104. (New) The method of claim 103, wherein the bone marrow aspirate is grown under hypoxia.
- 105. (New) The method of claim 103, wherein the growth medium comprises an effective amount of at least one angiogenesis stimulating cytokine selected from GM-CSF, MCP-1, EPAS1 and HIF-1.